Which flexible ureteroscope is the best for upper tract urothelial carcinoma treatment?

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Abstract: PURPOSE To present attributes of currently available flexible ureteroscopes to define the best flexible ureteroscope for upper tract urothelial carcinoma (UTUC) treatment. MATERIALS AND METHODS Scopus and Medline databases were searched for articles relating to performance of flexible ureteroscopes. A consensus for final inclusion of articles judged to be relevant for UTUC treatment was reached between the authors. Instrument characteristics were extracted from manufacturers' product brochures. RESULTS Smaller cross-sectional size of instruments is associated with increased probability for successful primary access to the upper urinary tract. The smallest flexible ureteroscopes are fiberoptic scopes. Smaller ureteroscopes also allow comparatively increased irrigation flow at constant intrarenal pressure. Digital flexible ureteroscopes achieve superior image quality compared to their fiberoptic counterparts, at the price of lower end-deflection ability. Image enhancement technologies such as narrow-band imaging (NBI), photodynamic diagnosis (PDD) and Image 1-S (formerly SPIES) are based on subjective image interpretation by the operator. NBI and PDD significantly increase tumor detection rate. The highest subjective image quality score of the Image 1-S technology is reached by the "Clara + Chroma" mode. Single-use ureteroscopes offer potential advantages over reusable scopes, including sterility, absence of contamination, immediate availability and exemption of previous instrument wear. CONCLUSIONS Miniaturization, digital image caption and image enhancement technologies seem to be the major determinants defining the best flexible ureteroscope for UTUC treatment. The impact of further factors, such as distal tip design, torque, working channel position, risk of contamination, as well as upcoming technological innovations should be evaluated in randomized controlled trials.

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Which flexible ureteroscope is the best for upper tract urothelial carcinoma treatment?

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Abstract

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Material and Methods: Scopus and Medline databases were searched for articles relating to performance of flexible ureteroscopes. A consensus for final inclusion of articles judged to be relevant for UTUC treatment was reached between the authors. Instrument characteristics were extracted from manufacturers' product brochures.

Results: Small cross-sectional size is associated with increased probability for successful primary access to the upper urinary tract. The smallest flexible ureteroscopes are fiberoptic scopes. Smaller ureteroscopes also allow comparatively increased irrigation flow at constant intrarenal pressure. Digital flexible ureteroscopes achieve superior image quality compared to their fiberoptic counterparts, at the price of lower end-deflection capacity. Image enhancement technologies such as narrow-band imaging (NBI), photodynamic diagnosis (PDD) and Image 1-S (formerly SPIES) are based on subjective image interpretation by the operator. NBI and PDD significantly increase tumor detection rate. The highest subjective image quality score of the Image 1-S technology is reached by the "Clara+Chroma" mode. Single-use ureteroscopes offer potential advantages over reusable scopes, including sterility, absence of contamination, immediate availability and exemption of previous instrument wear.

Conclusions: Miniaturization, digital image caption and image enhancement technologies seem to be the major determinants defining the best flexible ureteroscope for UTUC treatment. The impact of further factors, such as distal tip design, torque, working channel ~~size and~~ position, risk of contamination, as well as upcoming technological innovations should be evaluated in randomized-controlled trials.

Introduction

Upper urinary tract carcinoma (UTUC) is a rare malignancy with an incidence of 1-2/100'000 in western countries, accounting for 5-10% of all urothelial carcinomas [1-3]. Most cases of UTUC are invasive at diagnosis and the gold standard therapy is radical nephroureterectomy with bladder cuff excision [4].

Owing to technological improvements and refinement of surgical techniques, flexible ureteroscopy for UTUC has evolved from a diagnostic tool to a valid treatment alternative in well selected cases. This minimally-invasive retrograde approach was formerly reserved for imperative kidney-sparing UTUC treatment, but cumulative evidence has demonstrated its safe application to suspected or confirmed UTUC and has become a primary treatment option for patients with low-risk tumors (low-grade, unifocal and up to 2cm) [4,5].

While surgeons' skills significantly impact on the success of any surgical procedure, instrument features and characteristics are of particular relevance in ureteroscopy. This article presents attributes of currently available flexible ureteroscopes in order to define the best flexible ureteroscope for UTUC treatment.

Material and Methods

A non-systematic literature search was conducted using the Scopus and Medline databases, updated to December 2018. Original articles, reviews and editorials were selected based on their clinical relevance. Reference lists of selected manuscripts were checked manually for eligible articles. A consensus for final inclusion of articles judged to be relevant for UTUC treatment was reached between the authors. Additionally, ureteroscope product brochures were retrieved from manufacturers' websites and instrument characteristics were extracted from there.

Results

Handling characteristics

Anatomical considerations

The ureter is a helpful natural pathway for retrograde access to the upper urinary tract [6]. The downside of this natural pathway is the size-restriction dictated by three ureteral narrow portions: the ureteral orifice, the iliac vessels crossing and the pyeloureteral junction. These natural bottlenecks to ureteroscopy explain the necessity for miniaturized instruments.

Size, design and torque

The cross-sectional size of most currently available flexible ureteroscopes is ≤9F (Table 1), remarkably consistent with observations from a CT-scan-based analysis, where native ureteral diameter was ≤9F in 96% of all patients [7]. Overall, the smallest currently available flexible ureteroscopes are fiberoptic scopes, including the Olympus URF-P6 and URF-P7 as well as the Storz Flex X2 and Flex X2S (Table 1). When digital flexible ureteroscopes are considered separately, the smallest scopes are the Olympus URF-V2 and URF-V3 as well as the Storz Flex Xc (Table 1). No study to date evaluated whether miniaturized ureteroscopes may be more fragile and prone to damages compared to larger scopes.

Most ureteroscope manufacturers have opted for a tapered distal tip design, which allows for a substantial reduction of the cross-sectional size on the last millimeters of the distal instruments' end (Table 1) (Figure 1-A-B). Another design adjustment that may facilitate navigation in certain circumstances is the oval cross-sectional shape of instruments (Figure 1-C). Indeed, the ureter is not a cylindric tube, but rather a flaccid cavity that may potentially adapt to any cross-sectional instrument shape. Therefore, oval and round shaped cross-sectional tip designs may warrant different performance (e.g. primary insertion failure rate) according to the various anatomical characteristics. This concept needs to be addressed specifically in future studies.

The torque of a ureteroscope is often expressed as the ratio between rotation angle at the instrument's handle and shaft. No study available in literature yet evaluated whether ureteroscopes may differ based on torque abilities, although preliminary data suggest highest torque in favor of the Olympus URF-V2, followed by the Olympus URF-P6 and URF-P5 [8].

Primary flexible ureteroscopy

Primary flexible ureteroscopy should be considered for every retrograde approach to UTUC. Grasso et al. advocate a wireless and sheathless "no-touch" technique for primary diagnostic flexible ureteroscopy, in order to prevent instrumental artifacts that would compromise visual inspection of the urothelium [9]. Active ureteral dilation (e.g. balloon dilation) shall be regarded as a relative contraindication in cases of suspected or confirmed UTUC, since tumor seeding within deeper anatomical layers may occur when ureteral wall layers are disrupted. Consequently, postponement of ureteroscopy with ureteral stenting for passive dilation should be considered in cases of primary ureteroscope insertion failure.

Size, design and torque characteristics arguably may all impact on the ability of a given ureteroscope to warrant primary access to the upper urinary tract. A multicentric analysis including cases without prior ureteral dilation or prestenting reported about a primary insertion failure rate of <1% for 7.5F flexible ureteroscopes [10]. For 9.0F flexible ureteroscopes, primary insertion failure rate rose up to 37%. A more recent single-center analysis confirmed a low rate of insertion failure rate (1.4%) when 7.5F flexible ureteroscopes were used in unprepared ureteral units without active ureteral pathology [11]. Cross-sectional size of flexible ureteroscopes therefore appears a major factor impacting on ureteroscopic management of UTUC.

As for distal tip design and torque ability, no comparative study to date has evaluated the impact of these characteristics on primary insertion failure rate. Therefore, distal tip design and torque currently do not contribute to the choice for the best flexible ureteroscope for UTUC treatment.

Impact of ureteroscope size on irrigation flow

Smaller ureteroscopes also present an opportunity for better irrigation flow. Indeed, at constant intrarenal pressure, the main determinant of overall irrigation flow rate is irrigation outflow, which is dictated by the free space left between the outer contours of the ureteroscope and the inner wall of the ureter. The smaller the ureteroscope, the higher the outflow. This concept has been well illustrated in studies on ureteral access sheaths, which represent another alternative for increased irrigation outflow [12-14]. A compensatory rise of irrigation inflow can easily be achieved by increasing pressure of the irrigation fluid attached to the ureteroscope [15], although this should be performed with care since no ureteroscope to date can monitor intrarenal pressure.

Working channel size

The working channel size of currently available flexible ureteroscopes has been almost invariably maintained to 3.6F (Table 1). In that sense, flexible ureteroscopes do not differ in their ability to accept ancillary devices such as laser fibers, baskets, guide-wires and biopsy forceps. Therefore, working channel size does not contribute to the choice for the best flexible ureteroscope for UTUC treatment.

One exception are flexible ureteroscopes with a dual-channel design (Figure 1-B), which have been proposed to be advantageous when large cup forceps (e.g. the BIGopsy, Cook Medical, Bloomington, USA) are used for tissue biopsy [16]. The authors of this claim stipulate that the dual-channel design may offer enhanced flow properties. Considering the impact of relatively large dual-channel flexible ureteroscopes (9.9F) on irrigation outflow (see above), an enhanced irrigation inflow through the dual-channel ureteroscope would result in hazardously high intrarenal pressure [15]. At pressure levels higher than 80 cmH20, forniceal rupture may occur [17], and may be associated with a serious risk of perirenal tumor cell spillage. The true value of dual-channel flexible ureteroscopes in UTUC treatment should therefore be questioned.

Working channel position

Most flexible ureteroscopes have a working channel positioned at the 9 o'clock position of the field of view (Table 1). No study available to date evaluated the impact of the working channel position on management of UTUC, but it appears evident from daily clinical routine that certain lesions would become accessible to biopsy and laser-ablation if the working channel was positioned at the opposite side of the field of view. Consequently, if possible, it would be advisable to have at least two different types of ureteroscopes with opposed working channel positions on hold in the operating room whenever addressing UTUC by ureteroscopy. When performing laser treatment in a right-sided kidney, the calyces are seen on the left-side of the visualization screen. Therefore, a 3 o'clock working channel position is generally preferable to treat renal pelvic tumors in a right-sided kidney. For better access to tumors located in right anterior calyces, a 9 o'clock working channel position is recommended, such that the whole anteriorly located area becomes amenable to biopsy or laser-ablation [18]. Conversely, a 9 o'clock working channel is advised for left renal pelvic tumors, except for left posterior calyces where a 3 o'clock working channel is preferable.

Fiberoptic versus digital ureteroscopes

Flexible ureteroscopes were first based on the principles of optical glass fiber bundling, which were first described in 1954 by Harold H. Hopkins, a British physicist [19,20]. The light source was transmitted through a non-coherent bundle of optical fibers, while the image was transmitted through coherently organized optical fibers, with a corresponding optical fiber matrix of at both ends of the fiberscope. Each optical fiber was covered by a low-refraction index cladding for light transmission with minimal losses. These basic principles are still in use modern fiberoptic ureteroscopes.

Digital ureteroscopes rely on a fundamentally different image caption principle: electronic image sensors capture the digitalized image information at the tip of the instrument and transport the coded image signals over thin electronic wires for distant projection on a display (typically on a liquid crystal display (LCD)) [21]. These electronic image sensors (charge-coupled device (CCD) or complementary metal–oxide–semiconductor (CMOS) sensors) are composed of a matrix of photo-units (pixels) that capture primary colors (red, green and blue (RGB)), which produces a digital image after software processing.

The major advantages of digital image caption over fiberoptic image transmission are lower image quality losses and higher image resolution (bundles of ca. 10'000 – 20'000 optical fibers in last-generation fiberoptic flexible ureteroscopes against up to ca. 160'000 pixels in last-generation flexible digital ureteroscopes) (Figure 2).

In vitro studies confirmed superior image quality in favor of digital ureteroscopes [22,23]. This superiority may partly explain why digital ureteroscopes achieved significantly shorter operative time in several clinical studies on ureteroscopic stone treatment, when compared to fiberoptic scopes [24-26]. Most authors agree that digital ureteroscopes are superior for detection of UTUC, although this has not translated into lower recurrence rate to date [27].

Of note, electronic cables needed for image transport in digital ureteroscopes are several orders of magnitude smaller than bundled optical fibers in fiberoptic ureteroscopes. Theoretically, this may allow for a valuable cross-sectional instrument size reduction. Paradoxically, the thinnest currently available ureteroscope is a fiberoptic scope, as mentioned above (Table 1). This is caused by the relatively bulky architecture of currently available image sensor units at the tip of digital ureteroscopes, which have also been shown to cause substantial loss of end-deflection in a recent in-vitro study [28] (Figure 3).

Image enhancement technologies

Several real-time image enhancement technologies have been integrated to flexible ureteroscopes in an effort to improve diagnostic accuracy when managing UTUC: narrow-band imaging (NBI), photodynamic diagnosis (PDD) and Image 1-S technology (formerly SPIES). Other image enhancement technologies such as optical coherence tomography (OCT) and confocal laser endomicroscopy (CLE) are not detailed in this article, since those technologies involve the use of ancillary devices that can be inserted in any ureteroscope and therefore fall outside the study question of this manuscript.

Narrow-band imaging

NBI was first described in 1999 [29]. This technology involves color-filtering of the light emitted by the ureteroscope in order to illuminate tissues with two distinctive wavelengths: 415 nm (blue-violet) and 540 nm (green). Because these two wavelengths are strongly absorbed by hemoglobin [30], highly vascularized tissues appear darker than surrounding tissues. Additionally, the 540 nm light propagates deeper into tissues compared to the 415 nm light, which adds to contrasting of highly vascular tissues. Compared to white-light ureteroscopy, real-time NBI technology increased tumor detection rate by 22.7% in a study on 13 patients with suspected UTUC and 14 patients undergoing follow-up for known UTUC [31].

It is important to understand that the final image displayed on a LCD during NBI is rendered with a digitally reprocessed color scheme, since the light reflected by tissues is recorded as follows by the image sensor: the 415 nm wavelength (blue-violet light) is assigned to the blue and green color channel, while the 540 nm wavelength (green light) is assigned to the red color channel [29]. This explains the fluorescent-like blue-green appearance of normal mucosae, the brown-to-red appearance of superficial capillary networks (e.g. carcinoma in situ), as well as the cyan appearance of thicker blood vessels in papillary tumors ("frog eggs" appearance) and deeper connective tissues (Figure 4).

Of note, NBI requires an NBI-able light source and a corresponding NBI-able ureteroscope capable of digital reprocessing, as explained above. Currently, NBI is currently solely integrated to the Olympus URF-V, URF-V1 and URF-V2 (Table 1).

Photodynamic diagnosis

The PDD aims at revealing malignant tissues by fluorescence [32]. The most commonly employed fluorochromes are related to the heme-cycle, typically 5-aminolevulinic acid (5-ALA) and its derivate hexaminolevulinate (HAL). These fluorochromes particularly accumulate in malignant cells and can be excited by blue-violet light (380-470 nm) illumination from the ureteroscope. Upon relaxation, the fluorochrome emits a photon with a red-pink wavelength, thus exposing malignant tissue by a red-pink fluorescence.

This technology was originally explored for enhanced bladder cancer detection during cystoscopy and was later adapted to ureteroscopy for UTUC [32]. Somani et al. first reported about the use of real-time PDD in flexible ureteroscopy [33] and Kata et al. later thoroughly detailed their technique [34], which involves the use of a fiberoptic flexible ureteroscope, a PDD-able light source (emitting blue-violet light at 380-470 nm), a PDD-able camera and a long-pass filter (blocking light <450 nm) between the ureteroscope and the camera at the eyepiece in order to reduce the blue-violet background light from normal mucosa (380-470 nm). The authors of a recent systematic review came to the conclusion that PDD achieves significantly higher sensitivity and specificity for UTUC when applied to flexible ureteroscopy, with a particular advantage at detecting CIS and urothelial dysplasia [35]. In the largest available study to date, Kata et al. reported an increase of sensitivity from 54% to 96% and specificity from 95% to 97% between while-light and PDD ureteroscopy, respectively [36]. These promising results must be balanced against the technical requirements that currently may restrict this technology to expert centers with sufficient know-how for handling the above-mentioned operative setup.

While PDD may theoretically be applied to any fiberoptic ureteroscope by the use of a PDD-able light source and camera (Table 1), this technology has currently not been explored for digital ureteroscopy.

Image 1-S

The Image 1-S technology (formerly SPIES) offers real-time enhanced contrasting of digitalized images for better interpretation of images on LCD screens by the operator. This technology involves software-supported re-processing of the image captured by the digital image sensor and does not rely on a modified light source spectrum. Therefore, any light source can be used for illumination. The Image 1-S technology allows five re-processing modes, of which the "Clara+Chroma" mode has been shown to reach the highest subjective image quality score in recent in vitro studies [37,38]. Whether this improvement may impact on tumor detection rate during ureteroscopy has not been evaluated in any study to date.

The Image 1-S technology is currently solely integrated to the Storz Flex Xc (Table 1). Theoretically, this technology may be applied to any fiberoptic ureteroscope when an according Image 1-S camera is appended at the instrument's eyepiece, although at risk of lower image quality and potential loss of utility compared to the Storz Flex Xc.

Sterility and residual contamination

Several different processes for cleaning and sterilization of flexible ureteroscopes are proposed by manufacturers: manual cleaning and brushing of the working channel, as well as gas (ethylene oxide) or soaking disinfection (ethanol, glutaraldehyde, ortho-phthalaldehyde, etc…). Automated sterilization systems such as the Steris System 1 (washing and rising system with peracetic acid), the Steris V-PRO (vaporized hydrogen peroxide under vacuum conditions) and the Sterrad (hydrogen peroxide gas-based plasma sterilization) are also amenable to certain flexible ureteroscopes.

Only limited and outdated evidence on optimal scheduling of these cleaning and sterilization processes is available in literature [39,40]. Recent studies detailing sterilization processes of flexible ureteroscopes did not evaluate the grade of sterility and possible residual contamination, but rather reported on a possible association between sterilization processes and instrument damages [41-46]. Of note, there was a wide heterogeneity in cleaning and sterilization protocols in these studies.

In 2013, Chang et al. reported about an outbreak of ertapenem-resistant Enterobacter cloacae urinary tract infections due to a contaminated reusable ureteroscope [47]. The pathogen was only eliminated after gas sterilization (ethylene oxide) was added to the disinfection protocol. This report was followed by the findings of a study on manual cleaning and hydrogen-peroxide gas sterilization of 16 reusable ureteroscopes, which revealed microbial growth in 13%, adenosine triphosphate in 44%, hemoglobin in 63% and protein in 100% of all sampled ureteroscopes [48]. Comparatively, a new, unused ureteroscope was found without any contamination in that study.

There is currently no guidance on optimal cleaning and sterilization protocols and the recent reports on residual contamination raises the question whether reusable ureteroscopes might get contaminated by malignant cells after ureteroscopy for UTUC, and whether this may result in tumor seeding to other patients. In that sense, single-use ureteroscopes shall be considered a safe alternative to reusable ureteroscope whenever ureteroscopy is performed for UTUC.

Single-use ureteroscopes

Single-use ureteroscopes may vanish concerns about sterility and residual contamination encountered with reusable instruments, as discussed above [47,48]. Additionally, single-use ureteroscopes offer the advantage to be readily available and without traces of instrument wear, thus preventing postponement of interventions and warranting maximal performance (optical image quality, deflection range and torque) for each intervention [49]. In an evaluation of flexible ureteroscopes' weight, a single-use ureteroscopes was found substantially lighter compared to reusable scopes [50]. Such weight decrease has been associated with decreased muscle activity and may ultimately increase surgical productivity by preventing fatigue of the operator in favor of single-use ureteroscopes [51]. Finally, disposable instruments may cap the financial risks associated with sterilization processes and inadvertent breakage of scopes [41-46]. Regarding quality and performance characteristics, single-use ureteroscopes may compare to reusable flexible ureteroscopes, as presented in a recent in-vitro study [52].

Considering the above, single-use flexible ureteroscopes represent a major milestone of the past decade which has led to a complete rethinking of the operative room logistics and might be of advantage for UTUC treatment. Of note, performance of reusable ureteroscopes integrating image enhancement technology may still be superior in the setting of UTUC treatment to date.

Limitations

The level of evidence on the present topic was generally very low. Recommendations were mainly derived from retrospectively collected data. ~~There was a significant heterogeneity of study outcomes, and findings as well as recommendations were mainly derived from retrospectively collected data.~~ Future studies are warranted in order to evaluate how characteristics of flexible ureteroscopes may impact on UTUC treatment.

Conclusions

Miniaturization, digital image caption and image enhancement technologies seem to be the major determinants defining the best flexible ureteroscope for UTUC treatment. Single-use ureteroscopes may cap the theoretical risk of instrument contamination by malignant cells and warrant prompt availability of instruments with intact operational performance. The impact of further factors, such as distal tip design, torque, working channel ~~size and~~ position, as well as upcoming technological innovations should be evaluated in multicentric prospective randomized-controlled trials based on solid outcomes in order to define the best flexible ureteroscope for UTUC treatment.

Disclosures

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Authors' contribution

EXK: Project development, Data collection, Data analysis and Manuscript writing
SD: Data analysis and Manuscript editing
LV: Data analysis and Manuscript editing
OT: Project development, Data analysis and Manuscript editing

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

No informed consents were necessary for this study, since no research directly involving human participants and/or animals was performed in this study.

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Tables

Table 1: Characteristics of currently available flexible ureteroscopes

Figure Legends

Figure 1: Distal tip design. A: Round and tapered tip with single working channel (3.6F) and dual light source. B: Round and tapered tip with dual working channel (2.4F and 3.3F) and single light source. C: Oval and flat tip with single working channel (3.6F) and dual light source. Ureteroscopes were placed in a 12/14 ureteral access sheath for demonstration purposes.

Figure 2: Loss of end-deflection. A: Fiberoptic flexible ureteroscope. B: Digital flexible ureteroscope. Ureteroscopes were placed within in a plastic kidney model simulating a narrow-angle calyx (diameter of deflection: 18 mm). Projection of laser beam was illustrated by a red dotted line.

Figure 3: Image resolution. A: Image captured with a fiberoptic flexible ureteroscope. B: Image captured with a digital flexible ureteroscope.

Figure 4: Narrow-band imaging. A: Normal mucosae appears blue-green, while superficial capillary networks appear brown-to-red. B: “Frog eggs” appearance of a papillary tumor, with cyan appearance of tumorous vascular pedicles. C: Cyan appearance of thicker blood vessels under the mucosae.